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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,695	05/26/2006	Yasuhiko Tabata	3691-0122PUS1	9610

2292 7590 08/27/2008

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EXAMINER	
SASAN, ARADHANA	

ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
08/27/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/549,695	TABATA, YASUHIKO	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 05/12/08 are acknowledged.

2. Claim 2 was cancelled.

3. New claim 4 was added.

4. Claims 1 and 3-4 are included in the prosecution.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 1 remains rejected under 35 U.S.C. 102(b) as being anticipated by Ikada et al. (JP 08-325160).

The claimed invention is a sustained-release preparation which comprises a drug and a gelatin hydrogel. A concentration gradient of the drug is formed in the hydrogel.

Ikada teaches a crosslinked gelatin gel preparation "having long sustained releasability" and where a basophilic fibroblast growth factor (bFGF) is compounded with the gelatin gel (Abstract). A water solution of a bFGF is added to the gelatin gel preparation ([0005] and claim 11). The configuration of the gelatin gel is not limited and various shapes (cylindrical, prismatic, sheet, disk, globular, and particle) are disclosed [0009]. Since the gelatin gel will swell and degrade in the presence of water (or body

fluid) the concentration of the drug in the gel will change and consequently a concentration gradient of the drug in the gelatin gel will be formed.

The limitations of instant claim 1 are anticipated by the sustained release gelatin gel containing bFGF disclosed by Ikada (Abstract, [0005] and claim 11). The limitation of the concentration gradient of the drug that is formed in the hydrogel is an intrinsic feature of the drug containing gelatin gel as it swells and degrades in an aqueous environment.

7. Claim 3 remains rejected and new claim 4 is rejected under 35 U.S.C. 102(b) as being anticipated by Chvapil (US 4,485,088).

Chvapil teaches a method of delivering (in adult rats) a "lathyrogen across the skin barrier by sustained release from a bag made of a hydrogel polymer" (Col. 8, lines 59-61). The sustained release is shown in Table 2 where "during 120 hours of observation 22.5% of the drug penetrated across the skin and ... the release was continuous at the constant rate" (Col. 9, lines 5-24).

Therefore, the limitation of "a method of sustained release of a drug in vivo comprising administering a sustained release preparation to a patient in need thereof" of instant claim 3 is anticipated by the method of sustained release of a lathyrogen from a hydrogel polymer (Col. 8, lines 59-61 and Col. 9, lines 5-24). The topical administration limitation of instant claim 4 is anticipated by the delivery of a lathyrogen across the skin barrier as taught by Chvapil (Col. 8, lines 59-61).

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claim 1 remains provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10/484,023 ('023 hereinafter). Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims are drawn to a sustained-release preparation which comprises a drug and a bioabsorbable polymer hydrogel (a gelatin hydrogel) and claim 1 of '023 is also drawn to a sustained release gelatin hydrogel preparation. The difference is that claim 1 of '023 specifically includes a hepatocyte growth factor (HGF) in the gelatin hydrogel preparation. One having ordinary skill in the art at the time the invention was made would have found it obvious to include a drug such as HGF that could be used in a sustained release preparation. Since the instant claims are drawn to a drug containing sustained release

gelatin hydrogel preparation, they are obvious over the claim of '023 and thus they are not patentably distinct over each other.

10. Claim 1 remains provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10/528,998 ('998 hereinafter). Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims are drawn to a sustained-release preparation which comprises a drug and a bioabsorbable polymer hydrogel (a gelatin hydrogel) and claim 1 of '998 is also drawn to a sustained release gelatin hydrogel preparation. The difference is that claim 1 of '998 specifically includes an angiogenesis factor or a gene encoding the same in the gelatin hydrogel preparation. One having ordinary skill in the art at the time the invention was made would have found it obvious to include an active agent such as an angiogenesis factor or a gene encoding the same that could be used in a sustained release preparation. Since the instant claims are drawn to a drug containing sustained release gelatin hydrogel preparation, they are obvious over the claim of '998 and thus they are not patentably distinct over each other.

11. Claim 1 remains provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10/551,497 ('497 hereinafter). Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims are drawn to a sustained-release preparation which comprises a drug and a bioabsorbable polymer hydrogel (a gelatin hydrogel) and claim 1 of '497 is drawn to a gelatin hydrogel

that gradually releases HGF (hepatocyte growth factor) preparation. The difference is that claim 1 of '497 specifically includes HGF in the gelatin hydrogel preparation. One having ordinary skill in the art at the time the invention was made would have found it obvious to include an active agent such as HGF that could be used in a sustained or gradual release preparation. Since the instant claims are drawn to a drug containing sustained release gelatin hydrogel preparation, they are obvious over the claim of '497 and thus they are not patentably distinct over each other.

These are provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

Response to Arguments

Objection to the Specification

12. In light of Applicant's amendment to the Specification, the objection of 12/12/07 is withdrawn.

Rejection of claim 3 under 35 USC § 112, second paragraph

13. In light of Applicant's amendment of claim 3, the rejection of 12/12/07 is withdrawn.

Rejection of claims 1-2 under 35 USC § 102(b)

14. Applicant's arguments, see Page 5, filed 05/12/08, with respect to the rejection of claims 1-2 under 35 USC § 102(b) as being anticipated by Ikada et al. (JP 08-325160) have been fully considered but are not persuasive.

Applicant argues that the present invention has the advantage of a sustained release of the drug with control of direction of the drug release.

This is not found persuasive because instant claim 1 recites "a sustained release preparation". Ikada teaches a crosslinked gelatin gel preparation "having long sustained releasability" (Abstract). The sustained release of the drug with control of direction of the drug release is an inherent property of a sustained release gelatin gel preparation containing a drug. Moreover, it is noted that the features upon which applicant relies (i.e., control of direction of the drug release) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that the present invention has been misunderstood and that the Examiner likely envisages that the release of drugs occurs via a conventional diffusion mechanism. Applicant argues that with the conventional diffusion mechanism, even if a concentration gradient is present for a short period of time, the gradient is such that the surface portion is drug-lean (or poor) and the inner portion is drug-rich and that with this type of concentration gradient, the direction of the drug release cannot be controlled. Applicant argues that the characteristic feature of the gelatin hydrogel of the present invention is that the drug is entrapped (sustained) within the hydrogel via a physical interaction, for example an electrostatic interaction. Applicant argues that the present invention has the advantage of a sustained release of the drug with control of direction of the drug release wherein Ikada et al. does not disclose such a feature.

This is not persuasive because the features upon which applicant relies (i.e., the drug is entrapped within the hydrogel via a physical interaction, for example an

electrostatic interaction) are not recited in the rejected claim(s). Furthermore, diffusion may occur against a concentration gradient as well.

Therefore, the rejection of 12/12/07 is maintained.

Rejection of claim 3 under 35 USC § 102(b)

15. Applicant's arguments, see Page 9, filed 05/12/08, with respect to the rejection of claim 3 under 35 USC § 102(b) as being anticipated by Chvapil (US 4,485,088) have been fully considered but are not persuasive.

Applicant argues that Chvapil is related to a treatment of fibrosis during wound healing using hydrophilic hydrogel which allows the drug to be penetrated across the skin barrier and that Chvapil draws a conclusion that the drug is constantly released. Applicant argues that no gradient of the drug concentration will be made or maintained within the Chvapil gel.

This is not persuasive because diffusion may occur against a concentration gradient also.

Applicant's argument that Chvapil has the disadvantage of the release speed at the application site decreasing is not relevant because the release speed is not a claimed feature.

Therefore, the rejection of 12/12/07 is maintained.

Provisional Rejection of claim 1 under nonstatutory obviousness-type double patenting

16. Applicant's arguments, see Page 10, filed 05/12/08, with respect to the provisional rejection of claim 1 on the ground of nonstatutory obviousness-type double

patenting as being unpatentable over claim 1 of copending Application No. 10/484,023 ('023) have been fully considered but are not persuasive.

17. Applicant's arguments, see Page 10, filed 05/12/08, with respect to the provisional rejection of claim 1 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10/528,998 ('998) have been fully considered but are not persuasive.

18. Applicant's arguments, see Page 10, filed 05/12/08, with respect to the provisional rejection of claim 1 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10/551,497 ('497) have been fully considered but are not persuasive.

Applicant argues that claim 1 of each of the cited '023, '998 and '497 applications does not render claim 1 of the present application as obvious. Applicant argues that this is because the cited claims of the '023, '998 and '497 applications do not have a drug concentration gradient as achieved by the present invention. Applicant argues that the drug entrapped within the '023 / '998/'497 gelatin moves via diffusion (similar to the cited Ikada et al. reference mentioned above) and in the present invention, the direction of drug release is controlled and the drug is entrapped in the gel such that it will not move within the gel (i.e., no diffusion).

This is not found persuasive because the limitation of "the direction of drug release [that] is controlled" is not recited in instant claim 1. Instant claim 1 recites a concentration gradient of the drug that is formed in the hydrogel. One with ordinary skill in the art would know that diffusion may also occur against a concentration gradient.

Therefore, it would have been obvious to one of ordinary skill in the art to include different drugs in a sustained release preparation that comprises a sustained release gelatin hydrogel (as recited in claim 1 of each of the '023, '998 and '497 applications).

Therefore, the provisional obviousness type double patenting rejections of 12/12/07 are maintained.

Conclusion

19. No claims are allowed.

20. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
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